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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/439,311	11/12/1999	lANFONG H. LEE	78.560	1500

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/439,311	LEE ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 8-28* is/are pending in the application.

4a) Of the above claim(s) *2,8-15,26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,16-25,27-28* is/are rejected.

7)☒ Claim(s) *16,17,19 and 23* is/are objected to.

8)☐ Claim(s) *1-3 and 8-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 8-28 are pending.
Claims 2 and 26 (polypeptide), as well as claims 8-15 are stand withdrawn (methods), for reasons of record in paper number 5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 27, 2004 has been entered.

Please Note: The Examiner is reading newly amended independent claim 1, which now recites the phrase "said polynucleotide sequence consisting essentially of nucleotides 1-999 of the DNA sequence SEQ ID NO:1', to permit and encompass additional polynucleotides that encode a Campylobacter flaA immunogenic polypeptide that do Not change the "basic and novel" characteristic of the claimed composition. Since the phrase "consisting essentially of' permits the presence of additional components that do not change the "basic and novel" characteristic of the claimed composition and the basic and novel characteristic of the composition being claimed is a polynucleotide that encodes an immunogenic polypeptide of the flaA coding region of Campylobacter, the examiner is reading the claim to recite "open language".

The MPEP states "By using the term consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A consisting essentially of claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of' will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent

by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention". See also AK Steel Corp. v. Sollac, 344 F3.d 1234, 1239-1240, 68 USPQ2d 1280, 1283-84

Objections/Rejections Withdrawn

1. The disclosure is objected to because of the following informalities: page 19 is not longer objected to in light of the amendment of the specification removing the blank space.
2. Claims 1 and 16 rejected under 35 U.S.C. 102(e) as being anticipated by Meinersmann et al (US Pat. 5,837,825) is obviated through amendment of the claims to require N-terminal amino acid sequences not disclosed in Meinersmann et al.
3. Claim 1 rejected under 35 U.S.C. 102(e) as being anticipated by Schultz et al (US Pat. 6,270,874) has been obviated through amendment of the claims to require a minimum of 999 nucleotides.
4. Claims 1 and 3 rejected under 35 U.S.C. 102(b) as being anticipated by Alm et al (May 1993) has been obviated through amendment of the claims to require a minimum of 999 nucleotides.
5. Claims 1,3 and 16 rejected under 35 U.S.C. 112, first paragraph (New Matter), as failing to comply with the written description requirement has been obviated through amendment of the claims to recite the number of nucleotides encompassed by SEQ ID NO:1.
6. Claim 16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is herein withdrawn in light of newly submitted claim amendments, and new grounds of rejection.

Objections/Rejections Maintained

7. Claims 1,3, 16, 18,22, 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Logan et al (1989) for reasons of record.

Response to Arguments

8. The rejection of claims 1,3, 16, 18,22, 27-28 under 35 U.S.C. 102(b) as being anticipated by Logan et al (1989) is traversed on the grounds that:

   a. Logan et al fails to teach or enable one skilled in the art how to make and use the claimed invention.

9. It is the position of the examiner that Logan et al in the Materials and Methods section of the reference found on page 3031-3032 teaches how to make and use a bivalent attenuated

bacterial expression system that comprises a plasmid that encodes Campylobacter FlaA polypeptide, the polypeptide being encoded by a polynucleotide that comprises (consists essentially of, being read as open language) the recited range of nucleotides of SEQ ID No 1. (see Logan et al, page 3031, col. 2, paragraph 2, E.coli DH5, plasmid vector pBR322, E.coli GM2199 (an attenuated mutant strain of E.coli), living, grown in Luria medium). The reference anticipates the instantly claimed invention as now claimed.

New Grounds of Objection/Rejection

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 27 and 28 provides for the use of a polynucleotide sequence, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 27 and 28 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Objections

1. Claims 16-17, 19 and 23 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

2. Applicant states claim 16, (claim 17 depends from claim 16) is clear in light of the fact that claim 16 is directed to a specific polynucleotide sequence produced by a specific process or is recombinantly expressed in an expression system (Applicant's traversal is located at page 13, paragraph 2). In light of Applicant's comments stating that the polynucleotide is expressed in an expression system, defining the claimed composition as a polynucleotide in an expression vector, which is not the composition of claim 1, or claim 18 (isolated and purified) claims 16 ,17 and 19 are not further limiting of claim 1 and 18, respectively . This rejection could be obviated by amending the claim to recite: A recombinant expression vector system comprising the polynucleotide of claim 1 (or 18), wherein the polynucleotide is operatively linked and expressed in the expression vector system; or an equivalent expression that finds original descriptive support in the instant Specification.

Claim 23 depends from claim 22 and recites the phrase "an expression vector" rather than "said expression vector"; claim 23 recites a broader genus of expression vectors than those set forth in claim 22 through reciting any type of expression vector. Claim 23 is not further limiting of claim 23 through reciting a broader genus of expression vectors. This objection could be obviated by amending the claim to recite ------said expression vector of claim 22-------, or an equivalent phrase defining the expression vector to be one recited in claim 22.

Claim Rejections - 35 USC § 112

3. Claims 18-25, 27-28 are rejected under 35 U.S.C. 112, first paragraph, (scope) as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 18-25, 27-28 are directed to immunogenic compositions and the use of the polynucleotide to reduce colonization of Campylobacter and comprise any one or more of the following:

a. (claims 27 and 28) An isolated and purified flaA polynucleotide ,

b. (claims 18-25) a plasmid, or viral or E.coli expression system,

c. (claims 22-24) in association with a carrier strain.

The immunogenic/therapeutic composition of claims 18, 22,24 and 27-28 do not define any structural sequences, interactions, or interrelationships critical to the induction of an immune response. While claims 19-21 and 23 define a relationship between the flaA polynucleotides being fused to a second gene in an expression vector, the expression vectors defined in the base claim include plasmids and virus' that are not self replicating vectors and would not serve to induce an immune response to the encoded polypeptides in and of themselves. Assuming the plasmid or virus could be adsorbed or taken-up by a cell, the expression vectors are not so claimed to be vectors for expression of the encoded polypeptides in a eukaryotic cell, contained in an immunocompentent host animal.

Plasmids and viruses are not self-replicating microorganisms and would not serve as a self-contained expression system for the expression of the polynucleotide and induction of an immune response to the encoded polypeptide. The polynucleotide would need to be incorporated or introduced into a immunocompetant host cell for which the plasmid and viral vector were specifically adapted. The E.coli, Salmonella and Shigella expression vectors can serve as a self replicating expression systems, but the polynucleotide has not been incorporated into the

bacterial cells, and would therefore not serve to induce an immune response to the encoded Campylobacter FlaA polypeptide that flaA polynucleotides encodes.

The specification fails to provide an enabling disclosure for the preparation and use of any compositions, including viral vector compositions comprising nucleic acids encoding antigens because it fails to provide adequate guidance regarding how one would have prepared a nucleic acid which when introduced into a host would induce an immune response against the protein encoded by said nucleic acid. In contrast to direct protein immunogens, nucleic acids are required to target appropriate cell types within a host, become transcriptionally active, appropriately process any encoded proteins and present such proteins to the host in a manner suitable for recognition by the host's immune system. Such a **"gene therapy"** approach to epitope delivery suffers from all the limitations associated with gene therapy technology. However, as of 12/95, the artisan did not accept, in the absence of suitable and particular guidance, that such could have been accomplished without having had to have exercised undue experimentation. See e.g. NIH Report Reference.

4. Claims 16, 22, 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 encompasses the claimed isolated and purified polynucleotide that "is expressed" in a viral vector. As viral and plasmid vectors are not self-replicating microorganisms, the polynucleotide would not be expressed in the recited viral vector of claim 16. Though the claim recites the phrase "expression system", no other components are recited in the claim and therefore the vectors recited define the system; something is missing from the claim. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail

to provide adequate structural properties to allow for one to identify what is being claimed. Claim 16 is not further limiting of claim 1 from which it depends and does not clearly or distinctly claim Applicant's invention.

Claim 22 recites (paragraph 2) E.coli as and expression system and (paragraph 3) a carrier strain that will express the polynucleotide. How the E.coli expression system which is a type of carrier strain, and the bacterial carrier strain that will express the encoding polypeptide differ one from the other. What is bivalent about the immunogenic composition when the carrier strain and the E.coli expression system are one in the same system/carrier ? The invention is not distinctly claimed.

Claim 25 depends from claim 1 and recites the functional limitations of "said immunogenic polypeptide that has reduced or no induction of Guillain-Barre Syndrome". How the polynucleotide sequence of claim 1 differs structurally from the polynucleotide of claim 25 is not clearly or distinctly claimed. What has been modified or changed? . Claim 25 does not clearly or distinctly claim Applicant's invention based upon only reciting a functional limitation to define critical structural changes. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claim Rejections - 35 USC § 102

5. Claims 1, 3, 16, 18, 22, 24, 27-28 rejected under 35 U.S.C. 102(b) as being anticipated by Dumitru, Ioana (1995, dissertation).

Dumitru, Ioana disclose the instantly claimed invention directed to a bivalent immunogenic composition that comprises an E.coli (see Table 2.1, page 3)0or Salmonella attenuated (see section 1.1, pages 2-page 28, paragraphs 1-3) live bacteria strain (see title) transformed with an expression vector (see Table 2.2, pGEX-2T)
that comprises Campylobacter flaA coding sequence (see title) for a FlaA polypeptide (see page 24, section 1.2, paragraphs 2-3 and pages 25-26; page 27, paragraph 1).

The reference also discloses an isolated and purified polynucleotides, and a vector that comprises a portion of the coding sequence of the flaA gene (see page 34, paragraph 2, "coding for fla 1 gene with 258 bp missing at the C-terminus" in vector pGEX-2T), as well as pBlueF, a vector that comprises a polynucleotide that encodes for most of the FlaA protein (see page 34, paragraph 5, first two sentences) and additionally teaches the construction of fusion peptides between a desired polypeptide coding sequence and E.coli heat labile enterotoxin (see page 12, paragraph 1).

The reference discloses a fusion polynucleotide(see page 38, section 2.7), the polynucleotide comprising the sequence of flaA fused to the gene for GST (see abbreviations section page "x").

The reference anticipates the instantly claimed invention.

Conclusion

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.
7. US Pat. 5,494,795 (Guerry et al) is cited to show flaA portions of Campylobacter jejuni and coli DNA that encode polypeptides of flagellin.
8. Lee, LH et al, (1999) is cited to show a truncated recombinant flagellin subunit vaccine of Campylobacter jejuni.

9. Meinersmann et al (US Pat. 5,888,810) is cited to show a fusion gene between Campylobacter flagellin coding sequence together with an adjuvant coding sequence for E.coli LT-B (Heat labile enterotoxin).

10. Nuijten, P.J.M. et al (1990) is cited to show Campylobacter jejuni flagellin genes, as isolated DNA, in plasmids, helper phage and E.coli cells (see Experimental procedures, pages 17798 and 17799).

11. Pryor et al (1997) show fusion genes between a polynucleotide encoding a desired polypeptide and maltose binding protein (see page 310, col. 1, paragraph 1) in an analogous art for the purpose of showing an expression system with improved recovery of the desired polypeptide as compared to using glutathione S-transferase (see Table 2, "Yield" column, GST yield is 10 mg/L while maltose binding protein (pMAL) yield is 28-150 mg/l) .

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
September 2, 2004

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